

## **RAW SEQUENCE LISTING**

**The Biotechnology Systems Branch of the Scientific and Technical  
Information Center (STIC) no errors detected.**

Application Serial Number: 10/563,073  
Source: 1FWP  
Date Processed by STIC: 1/13/06

# ***ENTERED***



IFWP

## RAW SEQUENCE LISTING

DATE: 01/13/2006

PATENT APPLICATION: US/10/563,073

TIME: 10:27:40

Input Set : A:\pto.da.txt

Output Set: N:\CRF4\01132006\J563073.raw

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3 <110> APPLICANT: DOI, Hirofumi
4   SAITO, Ken
6 <120> TITLE OF INVENTION: Method of treating diabetes by inhibiting degradation of at
least one of
7   CREBL1, ATF6, and HNF-4 alpha by HtrA
9 <130> FILE REFERENCE: 3190-089
C--> 11 <140> CURRENT APPLICATION NUMBER: US/10/563,073
C--> 12 <141> CURRENT FILING DATE: 2005-12-29
14 <150> PRIOR APPLICATION NUMBER: PCT/JP2004/014377
15 <151> PRIOR FILING DATE: 2004-09-30
17 <150> PRIOR APPLICATION NUMBER: JP P2003-342587
18 <151> PRIOR FILING DATE: 2003-09-30
20 <160> NUMBER OF SEQ ID NOS: 35
22 <170> SOFTWARE: PatentIn version 3.1
24 <210> SEQ ID NO: 1
25 <211> LENGTH: 1377
26 <212> TYPE: DNA
27 <213> ORGANISM: Homo sapiens
29 <220> FEATURE:
30 <221> NAME/KEY: misc_feature
31 <223> OTHER INFORMATION: DNA that codes for HtrA2 precursor protein
34 <400> SEQUENCE: 1
35 atggctgcgc cgagggcggg gcggggtgca ggctggagcc ttcgggcatg gcgggctttg      60
37 gggggcattc gctgggggag gagacccgt ttgaccctg acctccgggc cctgctgacg      120
39 tcaggaactt ctgacccccg ggcccagtg acttatggga cccccagtct ctgggcccgg      180
41 ttgtctgttg gggctactga accccgagca tgccctgacgt ctgggacccc ggggtccccg      240
43 gcacaactga ctgcggtgac cccagatacc aggacccggg aggcctcaga gaactctgga      300
45 acccgttcgc gcgcgtggct ggcggtggcg ctgggcgctg ggggggcagt gctgttggtg      360
47 ttgtggggcg ggggtcgggg tcctccggcc gtcctcgccg ccgtccctag cccgccgccc      420
49 gcttctcccc ggagtcagta caacttcac gcagatgtgg tggagaagac agcacctgcc      480
51 gtggtctata tcgagatcct ggaccggcac cctttcttgg gccgcgaggt ccctatctcg      540
53 aacggctcag gattcgtggt ggctgccgat gggctcattg tcaccaacgc ccatgtggtg      600
55 gctgatcggc gcagagtccg tgtgagactg ctaagcggcg acacgtatga ggccgtggtc      660
57 acagctgtgg atcccgtggc agacatcgca acgctgagga ttcagactaa ggagcctctc      720
59 cccacgctgc ctctgggacg ctcagctgat gtccggcaag gggagtttgt tgttgccatg      780
61 ggaagtccct ttgcactgca gaacacgatc acatccggca ttgttagctc tgctcagcgt      840
63 ccagccagag acctgggact cccccaaacc aatgtggaat acattcaaac tgatgcagct      900
65 attgattttg gaaactctgg aggtcccctg gttaacctgg atggggaggt gattggagt      960
67 aacaccatga aggtcacagc tggaaatctcc ttgcccattc cttctgatcg tcttcgagag      1020
69 tttctgcata gtgggggaaaa gaagaattcc tcctccggaa tcagtgggtc ccagcggcgc      1080
71 tacattgggg tgatgatgct gacctgagt cccagcatcc ttgctgaact acagcttcca      1140
73 gaaccaagct ttcccgatgt tcagcatggt gtactcatcc ataaagtcat cctgggctcc      1200
75 cctgcacacc gggctgggtc gcggcctggt gatgtgattt tggccattgg ggagcagatg      1260
77 gtacaaaatg ctgaagatgt ttatgaagct gttcgaacct aatcccagtt ggcagtgcag      1320

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79 atccggcggg gacgagaaac actgacctta tatgtgaccc ctgagggtcac agaatga      1377
82 <210> SEQ ID NO: 2
83 <211> LENGTH: 458
84 <212> TYPE: PRT
85 <213> ORGANISM: Homo sapiens
87 <220> FEATURE:
88 <221> NAME/KEY: misc_feature
89 <223> OTHER INFORMATION: HtrA2 precursor protein
92 <400> SEQUENCE: 2
94 Met Ala Ala Pro Arg Ala Gly Arg Gly Ala Gly Trp Ser Leu Arg Ala
95 1          5          10          15
98 Trp Arg Ala Leu Gly Gly Ile Arg Trp Gly Arg Arg Pro Arg Leu Thr
99          20          25          30
102 Pro Asp Leu Arg Ala Leu Leu Thr Ser Gly Thr Ser Asp Pro Arg Ala
103          35          40          45
106 Arg Val Thr Tyr Gly Thr Pro Ser Leu Trp Ala Arg Leu Ser Val Gly
107          50          55          60
110 Val Thr Glu Pro Arg Ala Cys Leu Thr Ser Gly Thr Pro Gly Pro Arg
111 65          70          75          80
114 Ala Gln Leu Thr Ala Val Thr Pro Asp Thr Arg Thr Arg Glu Ala Ser
115          85          90          95
118 Glu Asn Ser Gly Thr Arg Ser Arg Ala Trp Leu Ala Val Ala Leu Gly
119          100         105         110
122 Ala Gly Gly Ala Val Leu Leu Leu Trp Gly Gly Gly Arg Gly Pro
123          115         120         125
126 Pro Ala Val Leu Ala Ala Val Pro Ser Pro Pro Ala Ser Pro Arg
127          130         135         140
130 Ser Gln Tyr Asn Phe Ile Ala Asp Val Val Glu Lys Thr Ala Pro Ala
131 145         150         155         160
134 Val Val Tyr Ile Glu Ile Leu Asp Arg His Pro Phe Leu Gly Arg Glu
135         165         170         175
138 Val Pro Ile Ser Asn Gly Ser Gly Phe Val Val Ala Ala Asp Gly Leu
139         180         185         190
142 Ile Val Thr Asn Ala His Val Val Ala Asp Arg Arg Arg Val Arg Val
143         195         200         205
146 Arg Leu Leu Ser Gly Asp Thr Tyr Glu Ala Val Val Thr Ala Val Asp
147         210         215         220
150 Pro Val Ala Asp Ile Ala Thr Leu Arg Ile Gln Thr Lys Glu Pro Leu
151 225         230         235         240
154 Pro Thr Leu Pro Leu Gly Arg Ser Ala Asp Val Arg Gln Gly Glu Phe
155         245         250         255
158 Val Val Ala Met Gly Ser Pro Phe Ala Leu Gln Asn Thr Ile Thr Ser
159         260         265         270
162 Gly Ile Val Ser Ser Ala Gln Arg Pro Ala Arg Asp Leu Gly Leu Pro
163         275         280         285
166 Gln Thr Asn Val Glu Tyr Ile Gln Thr Asp Ala Ala Ile Asp Phe Gly
167         290         295         300
170 Asn Ser Gly Gly Pro Leu Val Asn Leu Asp Gly Glu Val Ile Gly Val
171 305         310         315         320

```

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```

174 Asn Thr Met Lys Val Thr Ala Gly Ile Ser Phe Ala Ile Pro Ser Asp
175           325           330           335
178 Arg Leu Arg Glu Phe Leu His Arg Gly Glu Lys Lys Asn Ser Ser Ser
179           340           345           350
182 Gly Ile Ser Gly Ser Gln Arg Arg Tyr Ile Gly Val Met Met Leu Thr
183           355           360           365
186 Leu Ser Pro Ser Ile Leu Ala Glu Leu Gln Leu Arg Glu Pro Ser Phe
187           370           375           380
190 Pro Asp Val Gln His Gly Val Leu Ile His Lys Val Ile Leu Gly Ser
191 385           390           395           400
194 Pro Ala His Arg Ala Gly Leu Arg Pro Gly Asp Val Ile Leu Ala Ile
195           405           410           415
198 Gly Glu Gln Met Val Gln Asn Ala Glu Asp Val Tyr Glu Ala Val Arg
199           420           425           430
202 Thr Gln Ser Gln Leu Ala Val Gln Ile Arg Arg Gly Arg Glu Thr Leu
203           435           440           445
206 Thr Leu Tyr Val Thr Pro Glu Val Thr Glu
207           450           455

```

210 &lt;210&gt; SEQ ID NO: 3

211 &lt;211&gt; LENGTH: 981

212 &lt;212&gt; TYPE: DNA

213 &lt;213&gt; ORGANISM: Homo sapiens

215 &lt;220&gt; FEATURE:

216 &lt;221&gt; NAME/KEY: misc\_feature

217 &lt;223&gt; OTHER INFORMATION: DNA that codes for mature HtrA2

220 &lt;400&gt; SEQUENCE: 3

```

221 atggcgcgtcc ctagccccgcc gcccgccttct ccccgaggatc agtacaactt catcgcagat      60
223 gtgggtggaga agacagcacc tgccgtgggtc tatatcgaga tcctggaccg gcaccctttc      120
225 ttgggcccgcg aggtccctat ctcgaaacggc tcaggattcg tgggtggctgc cgatgggctc      180
227 attgtcacca acgccccatgt ggtggctgat cggcgcagag tccgtgtgag actgctaagc      240
229 ggcgacacgt atgaggccgt ggtcacagct gtggatcccg tggcagacat cgcaacgctg      300
231 aggattcaga ctaaggagcc tctccccacg ctgcctctgg gacgctcagc tgatgtccgg      360
233 caaggggagt ttgttggtgc catgggaagt ccctttgcac tgcagaacac gatcacatcc      420
235 ggcattgtta gctctgctca gcgtccagcc agagacctgg gactccccca aaccaatgtg      480
237 gaatacattc aaactgatgc agctattgat tttggaaact ctggagggtcc cctggttaac      540
239 ctggatgggg aggtgattgg agtgaacacc atgaagggtc cagctggaat ctcccttgcc      600
241 atcccttctg atcgtcttcg agagtttctg catcgtgggg aaaagaagaa ttcctcctcc      660
243 ggaatcagtg ggtcccagcg gcgctacatt ggggtgatga tgctgaccct gagtcccagc      720
245 atccttgctg aactacagct tcgagaacca agctttcccg atgttcagca tgggtgtactc      780
247 atccataaag tcatcctggg ctcccctgca caccgggctg gtctgcggcc tgggtgatgtg      840
249 attttggcca ttggggagca gatggtacaa aatgctgaag atgtttatga agctgttcga      900
251 acccaatccc agttggcagt gcagatccgg cggggacgag aaacactgac cttatatgtg      960
253 acccctgagg tcacagaatg a

```

256 &lt;210&gt; SEQ ID NO: 4

257 &lt;211&gt; LENGTH: 326

258 &lt;212&gt; TYPE: PRT

259 &lt;213&gt; ORGANISM: Homo sapiens

261 &lt;220&gt; FEATURE:

262 &lt;221&gt; NAME/KEY: misc\_feature

## RAW SEQUENCE LISTING

DATE: 01/13/2006

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TIME: 10:27:40

Input Set : A:\pto.da.txt

Output Set: N:\CRF4\01132006\J563073.raw

263 &lt;223&gt; OTHER INFORMATION: mature HtrA2

266 &lt;400&gt; SEQUENCE: 4

```

268 Met Ala Val Pro Ser Pro Pro Pro Ala Ser Pro Arg Ser Gln Tyr Asn
269 1          5          10          15
272 Phe Ile Ala Asp Val Val Glu Lys Thr Ala Pro Ala Val Val Tyr Ile
273          20          25          30
276 Glu Ile Leu Asp Arg His Pro Phe Leu Gly Arg Glu Val Pro Ile Ser
277          35          40          45
280 Asn Gly Ser Gly Phe Val Val Ala Ala Asp Gly Leu Ile Val Thr Asn
281          50          55          60
284 Ala His Val Val Ala Asp Arg Arg Arg Val Arg Val Arg Leu Leu Ser
285 65          70          75          80
288 Gly Asp Thr Tyr Glu Ala Val Val Thr Ala Val Asp Pro Val Ala Asp
289          85          90          95
292 Ile Ala Thr Leu Arg Ile Gln Thr Lys Glu Pro Leu Pro Thr Leu Pro
293          100         105         110
296 Leu Gly Arg Ser Ala Asp Val Arg Gln Gly Glu Phe Val Val Ala Met
297          115         120         125
300 Gly Ser Pro Phe Ala Leu Gln Asn Thr Ile Thr Ser Gly Ile Val Ser
301          130         135         140
304 Ser Ala Gln Arg Pro Ala Arg Asp Leu Gly Leu Pro Gln Thr Asn Val
305 145         150         155         160
308 Glu Tyr Ile Gln Thr Asp Ala Ala Ile Asp Phe Gly Asn Ser Gly Gly
309          165         170         175
312 Pro Leu Val Asn Leu Asp Gly Glu Val Ile Gly Val Asn Thr Met Lys
313          180         185         190
316 Val Thr Ala Gly Ile Ser Phe Ala Ile Pro Ser Asp Arg Leu Arg Glu
317          195         200         205
320 Phe Leu His Arg Gly Glu Lys Lys Asn Ser Ser Ser Gly Ile Ser Gly
321          210         215         220
324 Ser Gln Arg Arg Tyr Ile Gly Val Met Met Leu Thr Leu Ser Pro Ser
325 225         230         235         240
328 Ile Leu Ala Glu Leu Gln Leu Arg Glu Pro Ser Phe Pro Asp Val Gln
329          245         250         255
332 His Gly Val Leu Ile His Lys Val Ile Leu Gly Ser Pro Ala His Arg
333          260         265         270
336 Ala Gly Leu Arg Pro Gly Asp Val Ile Leu Ala Ile Gly Glu Gln Met
337          275         280         285
340 Val Gln Asn Ala Glu Asp Val Tyr Glu Ala Val Arg Thr Gln Ser Gln
341          290         295         300
344 Leu Ala Val Gln Ile Arg Arg Gly Arg Glu Thr Leu Thr Leu Tyr Val
345 305         310         315         320
348 Thr Pro Glu Val Thr Glu
349          325

```

352 &lt;210&gt; SEQ ID NO: 5

353 &lt;211&gt; LENGTH: 981

354 &lt;212&gt; TYPE: DNA

355 &lt;213&gt; ORGANISM: Artificial

357 &lt;220&gt; FEATURE:

## RAW SEQUENCE LISTING

DATE: 01/13/2006

PATENT APPLICATION: US/10/563,073

TIME: 10:27:40

Input Set : A:\pto.da.txt

Output Set: N:\CRF4\01132006\J563073.raw

358 <223> OTHER INFORMATION: Polynucleotide consisting of the same base sequence of SEQ ID NO:

359 3 wherein the nucleotide of position 520 is g

361 <220> FEATURE:

362 <221> NAME/KEY: misc\_feature

363 <223> OTHER INFORMATION: DNA that codes for mature HtrA2(S306A)

366 <400> SEQUENCE: 5

```

367 atggccgctcc ctagcccgcc gcccgtttct ccccgagctc agtacaactt catcgcagat    60
369 gtggtggaga agacagcacc tgccgtgggtc tatatcgaga tccctggaccg gcaccctttc    120
371 ttggggccgcg aggtccctat ctgcaacggc tcaggattcg tgggtggctgc cgatgggctc    180
373 attgtcacca acgcccctgt ggtggctgat cgccgcagag tccgtgtgag actgctaagc    240
375 ggcgacacgt atgaggccgt ggtcacagct gtggatcccc tggcagacat cgcaacgctg    300
377 aggattcaga ctaaggagcc tctccccacg ctgcctctgg gacgctcagc tgatgtccgg    360
379 caaggggagt ttgttgttgc catgggaagt ccccttgac tgcagaacac gatcacatcc    420
381 ggcattgtta gctctgctca gcgtccagcc agagacctgg gactccccca aaccaatgtg    480
383 gaatacattc aaactgatgc agctattgat tttggaaacg ctggaggtcc cctggttaac    540
385 ctggatgggg aggtgattgg agtgaacacc atgaagggtc cagctggaat ctcccttgcc    600
387 atcccttctg atcgtcttcg agagtctctg catcgtgggg aaaagaagaa ttcctcctcc    660
389 ggaatcagtg ggtcccagcg gcgctacatt ggggtgatga tgctgaccct gagtcccagc    720
391 atccttgctg aactacagct tcgagaacca agctttcccg atgttcagca tgggtgtactc    780
393 atccataaag tcatcctggg ctcccctgca caccgggctg gtctgcggcc tgggtgatgtg    840
395 attttggcca ttggggagca gatggtacaa aatgctgaag atgtttatga agctgttcga    900
397 acccaatccc agttggcagt gcagatcccg cggggacgag aaacactgac cttatatgtg    960
399 acccctgagg tcacagaatg a                                     981

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402 <210> SEQ ID NO: 6

403 <211> LENGTH: 326

404 <212> TYPE: PRT

405 <213> ORGANISM: Artificial

407 <220> FEATURE:

408 <223> OTHER INFORMATION: Polypeptide consisting of the same amino acid sequence of SEQ ID

409 NO:4 wherein the 174th amino acid residue is substituted by Ala

411 <220> FEATURE:

412 <221> NAME/KEY: misc\_feature

413 <223> OTHER INFORMATION: mature HtrA2(S306A)

416 <400> SEQUENCE: 6

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418 Met Ala Val Pro Ser Pro Pro Pro Ala Ser Pro Arg Ser Gln Tyr Asn
419 1          5          10          15
422 Phe Ile Ala Asp Val Val Glu Lys Thr Ala Pro Ala Val Val Tyr Ile
423          20          25          30
426 Glu Ile Leu Asp Arg His Pro Phe Leu Gly Arg Glu Val Pro Ile Ser
427          35          40          45
430 Asn Gly Ser Gly Phe Val Val Ala Ala Asp Gly Leu Ile Val Thr Asn
431          50          55          60
434 Ala His Val Val Ala Asp Arg Arg Arg Val Arg Val Arg Leu Leu Ser
435 65          70          75          80
438 Gly Asp Thr Tyr Glu Ala Val Val Thr Ala Val Asp Pro Val Ala Asp
439          85          90          95
442 Ile Ala Thr Leu Arg Ile Gln Thr Lys Glu Pro Leu Pro Thr Leu Pro
443          100         105         110
446 Leu Gly Arg Ser Ala Asp Val Arg Gln Gly Glu Phe Val Val Ala Met

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RAW SEQUENCE LISTING ERROR SUMMARY  
PATENT APPLICATION: US/10/563,073

DATE: 01/13/2006  
TIME: 10:27:41

Input Set : A:\pto.da.txt  
Output Set: N:\CRF4\01132006\J563073.raw

Invalid Line Length:

The rules require that a line not exceed 72 characters in length. This includes spaces.

Seq#:1; Line(s) 6

Invalid <213> Response:

Use of "Artificial" only as "<213> Organism" response is incomplete,  
per 1.823(b) of New Sequence Rules. Valid response is Artificial Sequence.

Seq#:5,6,7,8,9,10,11,12,13,14,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33

**VERIFICATION SUMMARY**

DATE: 01/13/2006

PATENT APPLICATION: US/10/563,073

TIME: 10:27:41

Input Set : A:\pto.da.txt

Output Set: N:\CRF4\01132006\J563073.raw

L:11 M:270 C: Current Application Number differs, Replaced Current Application Number  
L:12 M:271 C: Current Filing Date differs, Replaced Current Filing Date